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(54) Apparatus for preparation of a medical infusion solution

(57) In apparatus for preparation of a medical infusion solution, especially for the treatment of the urema by means of haemofiltration or peritoneal dialysis, infusion concentrate from a container (9) is mixed in desired ratio with high purity water in a mixing tank (15), the mixing ratio is determined and controlled gravimetrically by a weighing machine (26) and control device (27) and the concentration is checked continuously through measurement of the electrical conductivity of the solution by a conductivity meter (17). The high purity water is additionally filtered by sterile filters (13, 39) and the desired infusion solution is filtered through an ultrafilter (20) to be free of pyrogens for in-line infusion into the patient. All apparatus components such as concentrate supply container (9), electromagnetic valves (V1 to V8), pumps (P1, P2), pressure meter (19), conductivity meter (17), ultrafilter (20), sterile filters (13, 39), weighing machine (26) and control and regulating device (27) are located in a frame (40). The mixing tank (15) loads the electrical weighing machine (26). The electrical control and regulating parts are controlled by a microprocessor.

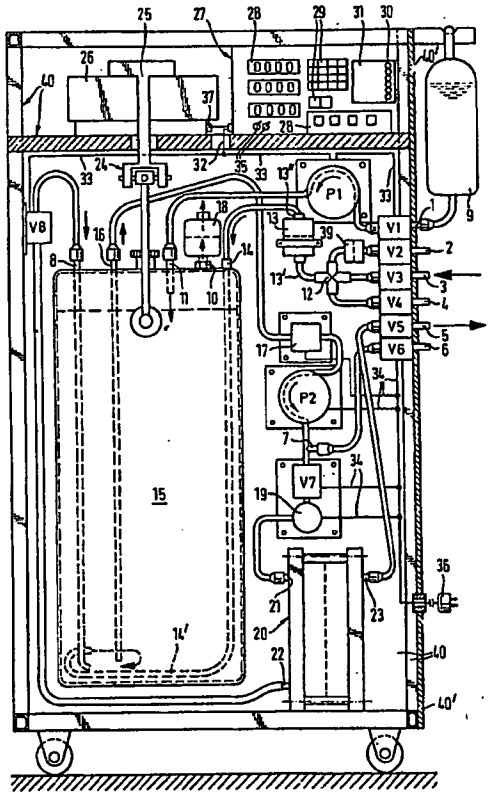

Fig. 1

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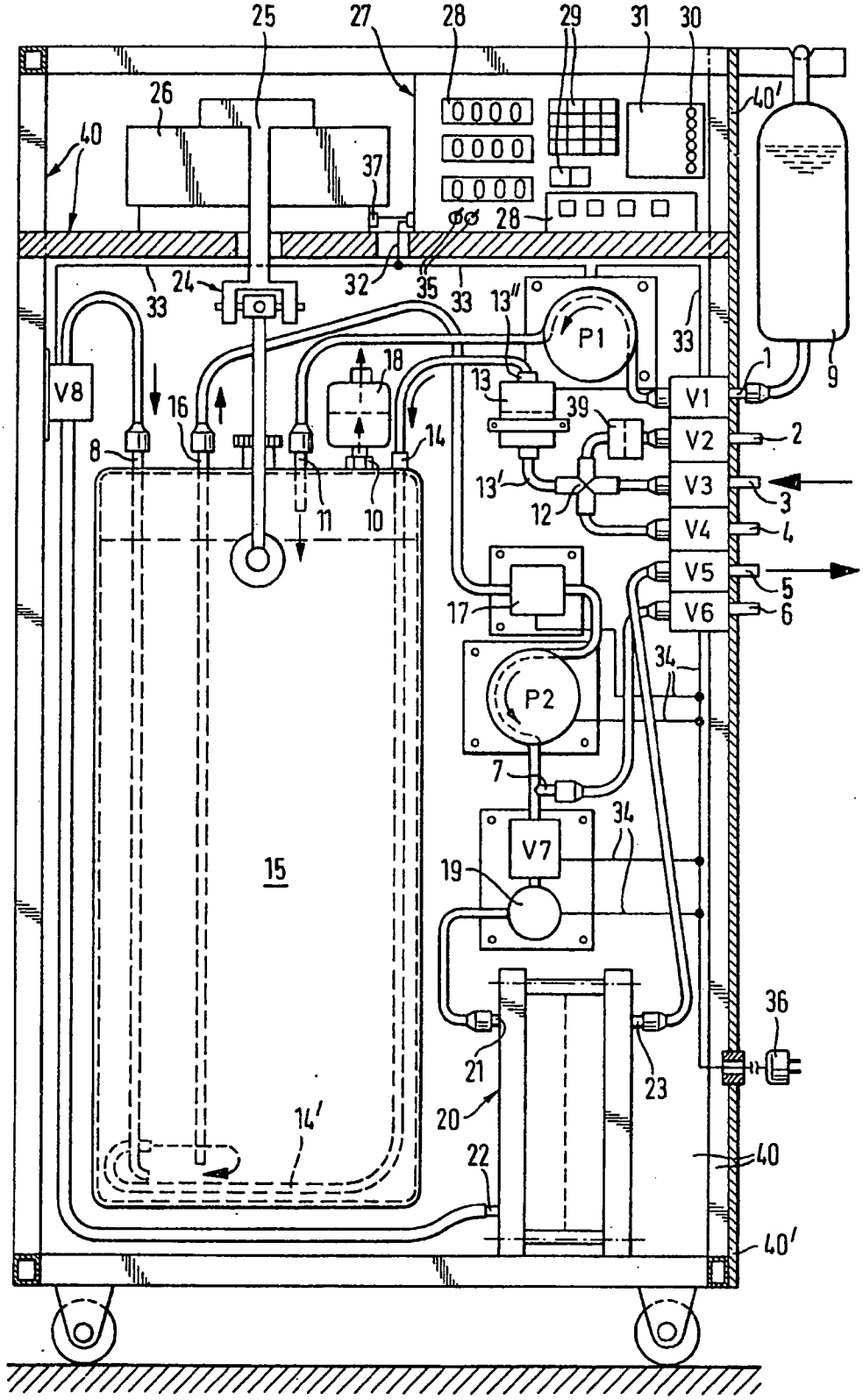
25
27
28
29
31
30
26
40
37
40'
28
32
35
33
24
33
13''
P1
33
V8
16
18
13
39
V1
V2
V3
V4
V5
V6
1
9
2
3
4
5
6
8
14
13'
12
11
10
17
34
P2
7
V7
34
19
15
36
21
23
20
14'
22
40
40'

Fig. 1

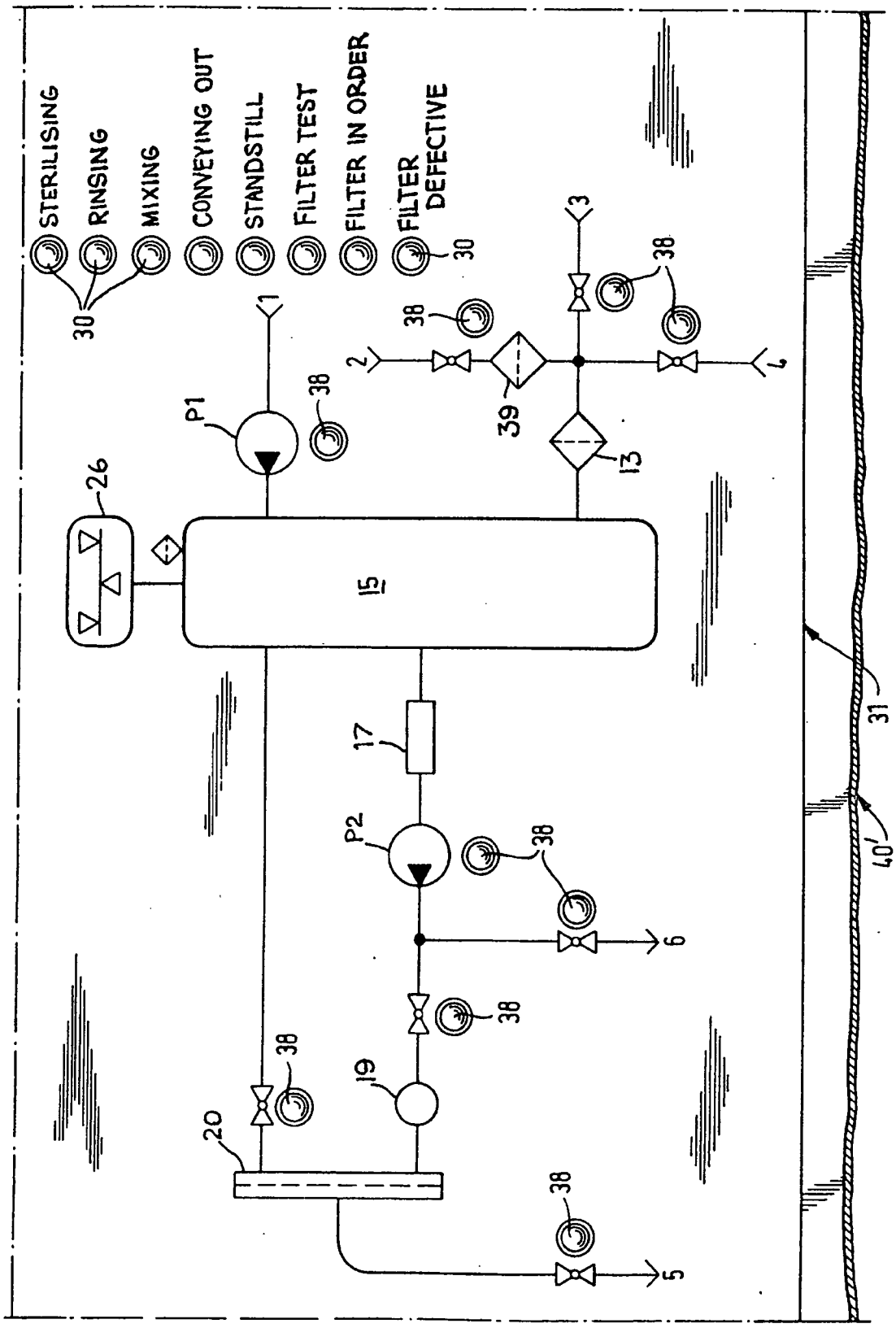
STERILISING
RINSING
MIXING
CONVEYING OUT
STANDSTILL
FILTER TEST
FILTER IN ORDER
FILTER DEFECTIVE
30
P1
P2
15
17
19
20
26
39
13
31
40
1
2
3
4
5
6
38

Fig. 2

SPECIFICATION

Apparatus for preparation of a medical infusion solution

The present invention relates to apparatus for preparation of a medical infusion solution.

Apart from haemodialysis, haemofiltration has in recent years gained ground as a method of treatment for acute and chronic kidney failure. GB—PS 1 563 840, US—PS 3 579 441, GB—PS 1 366 086, GB—PS 1 555 389 and US—PS 4 219 422 are referred to as exemplifying the state of the art. In such treatment, toxic substances amassed in the blood and an appreciable amount of blood liquid are withdrawn from the patient through filtration, the toxic substances and liquid being disposed of. At least a part of the liquid must be supplied back to the patient in the form of infusion solutions. These infusion solutions are delivered, sterilised and sterilely packaged, in kits for direct consumption and are supplied directly by way of dialysis machines or haemofiltration machines to the patient during the treatment. Because of the appreciable quantities which each patient needs, this commercial form of the infusion solution is unsatisfactory in economic terms. In addition, the danger of bacterial formation in the solution exists over longer storage periods and the patient is thereby exposed to risk. Since a large number of such "artificial kidneys" is present in clinics and dialysis centres, the need for infusion solution is therefore very great. Moreover, in the case of medical treatment of patients with kidney disease by dialysis, particularly in the case of the peritoneal dialysis, there is a need for germ-free infusion or treatment solutions, particularly solutions prepared under medical conditions.

Installations for the direct production of the infusion solution from the individual components are already known, for example EP—A 1 00 42 939, but these operate too inaccurately for clinical use.

There is therefore a need for apparatus which is simple in operation, reliably constructed and affords the possibility of producing infusion solutions for direct patient use in desired concentration and composition.

According to the present invention there is provided apparatus for preparing a medical infusion solution from an infusion concentrate and high purity water, the apparatus comprising a mixing tank, a concentrate container connected at an outlet thereof to a concentrate inlet of the tank, first conveying means operable to convey concentrate from the container to the tank, weight sensing means for sensing the weight of concentrate in the tank, a high purity water inlet connected by way of first controllable valve means and a sterilisation filter to a water inlet of the tank, an ultrafilter connected at a solution inlet thereof to a solution outlet of tank, at a solution outlet thereof to a solution inlet of the tank, and at a filtrate outlet thereof to a filtered solution outlet of the apparatus by way of second controllable valve means, second conveying means operable to convey solution from the tank to the ultrafilter, checking means operable to check solution conveyed from the tank to the ultrafilter, control means to determine the mixing ratio of concentrate to high purity water in the tank with reference to the weight sensed by the sensing means and to control the first and second valve means, the first and second conveying means and the checking means, and common support means supporting all the aforesaid components of the apparatus.

For the use of such apparatus it is to be taken into consideration that all clinics and dialysis stations already have large installations by which high purity water is producible from a central water supply, operating on the principle of the inverse osmosis, and the high purity water necessary for the preparation of the infusion solution is thus available in great quantity. This obviates the need for storage and transport of the proportion of high purity water hitherto required for the commercially available kits of infusion solution ready for use.

Apparatus embodying the invention can be constructed to be portable and stocking of components of the solution is restricted to relatively small quantities of electrolyte concentrate. The infusion solution prepared in the apparatus can be supplied, shortly after its production, by way of a dialysis or haemofiltration machine to the patient. The supplied solution is pyrogen-free and germ-free.

In a preferred embodiment, apparatus for the preparation of medical infusion solutions, particularly for use in the treatment of the urema by haemofiltration of peritoneal dialysis, comprises a plurality of component units located directly or indirectly in a common frame. The component units include a concentrate reserve container for the infusion concentrate, the container opening by its outlet into a mixing tank, a concentrate pump arranged between the tank and the container and driven by an electric motor to convey concentrate into the tank, and a plurality of liquid coupling means arranged in combination with shut-off valves with electrically movable shut-off elements. One such coupling means forms a high purity water inlet for high purity water, produced by inverse osmosis or by other methods, from a high purity water reservoir, and opens into the entry of a sterile filter having a pore size of substantially 0.2 micrometres so as to retain bacteria, the exit of the filter opening into the mixing tank. An outlet of the tank opens into the inlet of an ultrafilter, which is located or supported on the frame and which has a cut-off of at most substantially 20000 Daltons so as to retain pyrogens, the outlet at the impure side of the ultrafilter opening into the tank. An electrical liquid pressure meter, a conveying pump driven by an electric motor, and an electrical conductivity meter for measurement of the actual concentration of the infusion solution are arranged between the outlet at the impure side of

the ultrafilter and the tank, while the outlet at the pure side of the ultrafilter opens into a tap and shut-off valve. The tank, standing or hanging in the frame, loads a force meter or a weighing machine located at the frame and an electrical control and regulating device is provided for balancing the mixing ratio of concentrate and high purity water, the device being equipped with a manual input keyboard, several function switches and pilot lamps, and alpha-numeric indicators and being arranged to control the electrical components units of the force meter or weighing machine, both the pumps, the shut-off and tap valves, the pressure meter and the concentration meter.

For preference, additional shut-off valves are arranged between the ultrafilter and the tank, and a bypass with a shut-off valve is arranged between the ultrafilter, the conveying pump and the mixing tank.

In addition, a cruciform current divider, the outlets of which open in further shut-off valves and in at least one further sterile filter of a pore side of substantially 0.2 micrometres, may be arranged between the sterile filter and the shut-off valve for the connection of the high purity water.

Expediently, the shut-off valves are electromagnetically controlled disphragm valves.

The mixing tank may also carry a filter for sterile aeration and ventilation at a further outlet.

Preferably, the apparatus frame has a casing which has passages of a size for lampholders, facing the outside of the apparatus, for signal lamps, signal lamps being arranged in the passages. A circuit symbol carrier may be arranged on the casing for the electrically controlled valves and both pumps and directly associated with a part of the signal lamps.

The water inlet of the mixing tank container can be constructed as an immersion pipe with a bent end portion promoting intermixing and ending at the tank base.

For protection against bacterial formation in the solution during longer term storage thereof, the outlet at the pure side of the ultrafilter can be connectible with the water inlet of the mixing tank, preferably with the inlet of the sterile filter, and the solution moved by the conveying pump in a recirculation circuit inside the apparatus from the tank by way of the ultrafilter and the sterile filter and back into the tank. Expediently, the outlet at the impure side of the ultrafilter is included in the shunt path of the ultrafilter and tank in the recirculation circuit maintained by the conveying pump. All liquid-conducting ducts and components groups can be connectible into a closed circuit rinsed through by a sterilising medium by fluid short-circuit of individual inlet and outlets of the valves and their selective blocking.

An embodiment of the present invention will now be more particularly described by way of example with reference to the accompanying drawings, in which:

Fig. 1 is a schematic elevation of portable apparatus embodying the present invention; and

Fig. 2 is a front view of part of a control panel of the apparatus.

Referring now to the drawings, there is shown apparatus for preparation of a medical infusion solution, the apparatus comprising individual components mounted on a frame 40 which is equipped with rollers and which is covered at least in places by a casing 40'.

The components essentially comprise shut-off valves V1 to V8, which at the inlet and outlet sides thereof are provided with self-blocking couplings for the reception of hoses, two pumps P1 and P2, an electrical conductivity meter 17, a liquid pressure meter 19, an ultrafilter 20. at least three sterile filters 13, 39 and 18, a mixing tank 15, a weighing machine 26 and a control and regulating device 27.

In the illustrated embodiment, the tank 15 is suspended by way of two universal joints 24 and a like 25 to freely hang from and to load the upper pan weighing machine 26. Alternatively, the weighing machine 26 can be arranged at the frame base, in which case the tank 15 can stand on the weighing machine. Instead of the weighing machine, other conventional force receivers can serve as gravimetric measurement value transmitters.

All remaining components are located through screw connections or the like indirectly or directly at the frame 40.

A concentrate reserve container 9 for an electrolyte concentrate hands from, for example, a gallows of the frame 40 and the container outlet is connected to the coupling 1 of the valve V1. The pump P1, driven by an electric motor, is arranged between the container 9 and the valve 1 and conveys concentrate into an inlet 11 of the tank 15. A connection with a high purity water reservoir (not shown) is provided by way of a hose at an inlet 3 of the valve V3. The outlet of the valve V3 is connected to a cruciform flow divider 12, the two take-off outlets of which are connected to the valve V2 and its coupling 2 and to the valve V4 and its coupling 4. The third outlet of the divider 12 is connected to an inlet 13' of the filter 13, which has a pore size of 0.2 micrometres and retains bacteria present in the high purity water. An outlet 13" of the filter 13 is connected to a further inlet 14 of the tank 15, which inlet, in order to promote intermixing, connects with an immersion pipe 14' ending in a circular or spiral shaped nozzle at the tank base. The filter 39, having a poure size of 0.2 micrometres, is arranged between the valve V2 and the divider 12.

An outlet 16 of the mixing tank 15 is connected to the electrical conductivity meter 17, which measures the electrical conductivity of the liquid in the tank 15, the conductivity being dependent on the actual concentration of the liquid. The exit of the the meter 17 opens in a T-shaped flow divider 7, which forms a bypass with the valve V6 and coupling 6. The divider 7 is also

connected with the valve V7 and an inlet 21 of the ultrafilter 20, the inlet having a diaphragm which retains pyrogens and has a cut-off of at most 20000 Daltons. The meter 17, the pump P2, the divider 7, the valve V7 and the liquid pressure meter 19 are all arranged between the inlet 21 of the ultrafilter 20 and the outlet 16 of the tank 15. According to the form of construction, liquid flows directly or indirectly through these component parts.

The outlet 22 at the impure side of the ultrafilter 20 is connected by way of the valve V8 with a further inlet 8 of the tank 15 and also ends in a circularly shaped portion at the tank base. The outlet 23 at the pure side of the ultrafilter 20 is connected to the valve V5 and the coupling 5. This coupling 5 serves as an outlet for the direct transmission of the prepared infusion solution to a container for intermediate storage or to a user or users, namely patients with kidney disease, with the interposition of a dialysis or haemofiltration machine.

The electrical control and regulating device 27 comprises a computer, a plurality of alpha-numeric indicators 28 in digital form as well as an input keyboard 29, pilot lamps 30 and a circuit diagram foil 31 or imprint, which is more closely explained in connection with Fig. 2. The electrical component parts of the weighing machine 26, the device 27, the pumps P1 and P2, the valves V1 to V8, and the meters 17 and 19 are electrically intercoupled by means of electrical lines 32, 33 and 34 and are connected or connectible by a plug 36 to a current mains. The device 27 also includes several function switches 35. The illustrated, commercially available weighing machine 26 is equipped with a microprocessor and connected through a data output 37 with the device 27.

The apparatus can be permanently connected by the valve V3 and coupling 3 to a high purity water source.

Before placing the apparatus in operation for preparation of an infusion solution, it must be sterilised and rinsed free of sterilising medium. In this case, chemical sterilisation by formalin or by a hot sterilisation process can take place. For this purpose, the chemical sterilisation medium is introduced in concentrated form by way of the coupling 1 and valve V1, all other valves being closed. The concentrated sterilisation medium is diluted with high purity water in the mixing tank according to a preselected mixing ratio.

The valve V1 is connected with the valve V2, and the valve V4 with the valve V5, by means of short connecting hoses. Thus, the entire duct system forms a closed circuit and all liquid-conducting component groups can be sterilised chemically through appropriate setting of the valves and pumps. A clock built into the apparatus indicates the duration of the sterilising.

After completion of the sterilising, the sterilisation medium is discharged by way of the bypass 7 and the coupling 6. The entire duct system is rinsed free, through appropriate setting of the valves, of sterilising medium residues by high purity water, the number of the rinsing cycles being displayed.

The tank 15 holds about 50 litres of liquid. For the production of a certain quantity of infusion solution, there is selected by way of the device 27 firstly the desired volumetric mixing ratio (concentrate/high purity water), secondly the specific weight of the concentrate (the specific weight of the high purity water is set automatically at 1 gram per millilitre by the computer of the device 27) and thirdly the total quantity of the solution to be produced.

Thereafter, any liquid remaining in the apparatus is discharged by way of the coupling 6.

Since the mixing ratio, as is usual in the dialysis, is selected volumetrically, the corresponding gravimetric mixing ratio is automatically calculated by the computer with reference to the specific weight of the concentrate. The calculated quantity of concentrate is metered by the pump P1 into the empty tank 15, the pump P1 stopping when the target weight is reached. In the rest state, the weight of concentrate is determined exactly by weighing. Should a difference exist between the target weight and the actual weight of the concentrate, the quantity of high purity water to be conveyed is calculated anew according to the actual weight of concentrate. By this means, an exact setting of the mixing ratio is ensured. The valve V3 then opens and high purity water flows via this valve and the filter 13 through the immersion pipe 14' into the tank 15, the pipe 14' being so constructed that a circular vortex and thereby a homogeneous intermixing of the water and concentrate takes place in the tank. The valve V3 closes when the calculated quantity has flows into the tank. The pump P2 then starts and the valve V8 is opened (all other valves are closed). As a result, an additional intermixing of the infusion solution is achieved, the impure side of ultrafilter 20 is freed of air and the surface of the ultrafilter 20 is cleaned. The mixing program is thereby concluded.

A quantity of the infusion solution, which for example is to be filled into an inspection bag, can be preselected by way of the keyboard 29. This quantity is conveyed out of the tank 15 by the pump P2, checked for exact concentration by the meter 17 and filled into a vessel through the ultrafilter 20 and the valve V5. On deviation of the conductivity from a target value, the valve V5 closes and the solution is rejected by way of the bypass 7. The rejected quantity is not counted towards the quantity filled.

The apparatus possesses a special program for protection against bacterial formation during extended periods of non-withdrawal of infusion solution from the apparatus. For this purpose, the valve V4 is connected with the valve V5 by means of a hose connection. The pump P2 maintains a liquid flow which circulates from the tank 15 by way of the pump P2, ultrafilter 20, valves V5 and V4 and filter 13 back into the tank 15. For this

purpose the outlet 23 of the ultrafilter 20 and the valve V5 are connected with the inlet 14 of the tank 15, preferably with the valve V4, and the inlet 13' of the filter 13 and the prepared infusion solution is conveyed by the pump P2 in a circulation circuit inside the apparatus from the tank 15 by way of the ultrafilter 20 and filter 13 back to the tank. The outlet 22 of the ultrafilter 20 is in that case included in the shunt path of ultrafilter and tank in the recirculation circuit maintained by the pump P2.

Also present in the apparatus is an aeration filter 18 which is placed on a further outlet 10 of the tank 15 and which serves for sterile aeration and ventilation of the tank.

The operating and indicating elements of the control and regulating device 27 are integrated into the apparatus casing as is the foil 31, which through electric lamps optically indicates the actual operating stage of the apparatus in the individual switching phases and is shown in more detail in Fig. 2. The circuit diagram is printed on a film or drawn directly on the apparatus casing. Arranged beside the symbols for the electrical components influenced by the device 27, namely the pumps P1 and P2 and the valves V1 to V8, are passages in which small signal lamps are fastened. These contact the device 27 and indicate the operating stage through their switched-on or switched-off state. These signal lamps are designated uniformly by 30 and 38 in Fig. 2. Due to this arrangement, the operator is able to visually follow the actual program run-down and the control of the valves and other electrical component units and to immediately recognise possible errors or failures.

CLAIMS

1. Apparatus for preparing a medical infusion solution from an infusion concentrate and high purity water, the apparatus comprising a mixing tank, a concentrate container connected at an outlet thereof to a concentrate inlet of the tank, first conveying means operable to convey concentrate from the container to the tank, weight sensing means for sensing the weight of concentrate in the tank, a high purity water inlet connected by way of first controllable valve means and a sterilisation filter to a water inlet of the tank, an ultrafilter connected at a solution inlet thereof to a solution outlet of tank, at a solution outlet thereof to a solution inlet of the tank, and at a filtrate outlet thereof to a filtered solution outlet of the apparatus by way of second controllable valve means, second conveying means operable to convey solution from the tank to the ultrafilter, checking means operable to check solution conveyed from the tank to the ultrafilter, control means to determine the mixing ratio of concentrate to high purity water in the tank with reference to the weight sensed by the sensing means and to control the first and second valve means, the first and second conveying means and the checking means, and common support means supporting all the aforesaid components of the apparatus.

2. Apparatus as claimed in claim 1, the support means comprising a frame.

3. Apparatus as claimed in either claim 1 or claim 2, the first and the second conveying means each comprising a pump and an electric motor to drive the pump.

4. Apparatus as claimed in any one of the preceding claims, the sensing means being arranged to support the mixing tank and comprising one of a weighing machine and a force meter.

5. Apparatus as claimed in any one of the preceding claims, wherein the sterilisation filter has a pore size of substantially 0.2 micrometres.

6. Apparatus as claimed in any one of the preceding claims, the ultrafilter having a cut-off of at most substantially 20000 Daltons.

7. Apparatus as claimed in any one of the preceding claims, the checking means comprising a liquid pressure meter and an electrical conductivity meter.

8. Apparatus as claimed in any one of the preceding claims, the control means comprising a manual input keyboard, a plurality of control switches and pilot lamps and alpha-numeric indicating means.

9. Apparatus as claimed in any one of the preceding claims, comprising third controllable valve means arranged in the connection between the solution outlet of the tank and the solution inlet of the ultrafilter and fourth controllable valve means arranged in the connection between the outlet of the ultrafilter and the solution inlet of the tank.

10. Apparatus as claimed in claim 9, comprising a bypass duct connected between the third valve means and fifth controllable valve means.

11. Apparatus as claimed in any one of the preceding claims, comprising flow take-off means arranged in the flow path between the first valve means and the sterilisation filter and connected at one take-off thereof to respective controllable valve means and at another take-off thereof to respective controllable valve means by way of a further sterilisation filter.

12. Apparatus as claimed in claim 1, wherein the further sterilisation filter has a pore size of substantially 0.2 micrometres.

13. Apparatus as claimed in any one of the preceding claims, each of the valve means comprising an electrically controllable shut-off valve and associated duct coupling means.

14. Apparatus as claimed in claim 13, each of the valves comprising an electromagnetic diaphragm valve.

15. Apparatus as claimed in any one of the preceding claims, wherein the tank is provided with a ventilation outlet connected to a sterilising aeration filter.

16. Apparatus as claimed in any one of the preceding claims, the support means comprising a casing and the control means comprising a plurality of signal lamps mounted in openings in

the casing and a diagram carrier which is arranged on the casing in association with the signal lamps and which carries a circuit diagram for the valve means and the conveying means.

17. Apparatus as claimed in any one of the preceding claims, wherein the water inlet of the mixing tank is provided by an immersion pipe which extends in the tank to end in the region of the base thereof and which is shaped to discharge water in the tank in a current promoting intermixture with the concentrate.

18. Apparatus as claimed in any one of the preceding claims, the second valve means being connectible to the water inlet of the mixing tank and the second conveying means being controllable by the control means to circulate prepared solution on a circulation path through the tank by way of the solution outlet and water inlet thereof, the ultrafilter, the second valve means and the sterilisation filter between the second valve means and the water inlet of the tank thereby to keep the solution in movement for prevention of bacterial formation.

19. Apparatus as claimed in claim 18 when appended to claim 11, the second valve means being connectible to the tank water inlet by way of said respective valve means connected to said one take-off of the flow take-off means.

20. Apparatus as claimed in either claim 18 or claim 19, wherein the part of the circulation path through the tank is additionally by way of the solution inlet of the tank.

21. Apparatus as claimed in any one of the preceding claims, wherein the valve means, the inlets and the outlets are so interconnectible and controllable as to provide a closed circuit path through all liquid-conducting components of the apparatus for circulation of a sterilising medium.

22. Apparatus substantially as hereinbefore described with reference to the accompanying drawings.

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